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# Nanotechnology in Medicine: Targeted Drug Delivery Systems

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## ABSTRACT

Nanotechnology has revolutionized the field of medicine by enabling the precise manipulation of materials at the atomic and molecular levels, leading to the development of highly efficient targeted drug delivery systems. These systems enhance therapeutic efficacy, minimize side effects, and improve patient compliance. This paper explores the fundamentals of nanotechnology, the architecture of drug delivery systems, and the role of nanocarriers both organic and inorganic in therapeutic applications. Special attention is given to targeted delivery mechanisms, surface modifications for improved biocompatibility, and recent advancements in cancer and gene therapies. Despite significant preclinical successes, clinical translation remains challenged by biological barriers, manufacturing complexity, and regulatory hurdles. Future directions suggest a paradigm shift toward smart, multifunctional nanomaterials designed for precision medicine. This review underscores the critical need for multidisciplinary collaboration to overcome existing challenges and to fully realize the clinical potential of nanotechnology in targeted drug delivery.

Keywords: Nanotechnology, Targeted Drug Delivery, Nanocarriers, Cancer Therapy, Gene Therapy, Surface Modification.

## INTRODUCTION

Nanotechnology is a cutting-edge science field focused on manipulating materials on an atomic or molecular scale (1-3 nm), equivalent to a few thousand atoms or angstroms. It aims to revolutionize science by producing goods with superior properties and enabling low-cost mass fabrication. This interdisciplinary field spans various domains, including biomolecular chemistry, bioengineering, molecular nanocomputing, and innovative medical applications. Nanoscale materials showcase unique optical, mechanical, and electrical properties due to their size and shape, leading to smart device development. Current applications include cosmetics, self-cleaning surfaces, and water repellants, with ongoing discoveries. In medicine, nanotechnology enhances drug delivery, allowing for efficient, targeted treatments. The method of administration affects patient treatment outcomes. Oral delivery, preferred for systemic effects, involves tablets or capsules that are changed in the digestive system before absorption. Topical applications target specific epithelial tissues, using surface application or inhalation to reach deeper lung tissues. Intravenous administration quickly introduces drugs directly to the bloodstream, common in clinical settings for insulin or blood factor adjustments. Nanocarriers can facilitate the controlled release of medications like losartan for chronic ailments. Rectal administration is also practical for infants or those with frequent vomiting. Inhalation therapy is particularly beneficial for patients with asthma or respiratory conditions, though timing challenges may arise with traditional vitamin tablets [1, 2].

### Overview of Drug Delivery Systems

Drug delivery systems encompass the intricate processes involved in the efficient storage of therapeutic drugs and their effective penetration through various biological barriers to successfully reach specific targeted tissues or organs within the human body. These sophisticated systems are primarily classified

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into three major categories: macromolecule systems, particulate solid systems, and eye-drop delivery systems. The role of biomaterials is critical in the overall process of drug storage and subsequent delivery. Among these systems, nanocarriers, which can be sized anywhere from 1 to 1000 nanometers, represent advanced micro- and nano-drug delivery systems that are meticulously crafted from a diverse range of materials, including polymers, lipids, proteins, and both metal and silica nanoparticles. The significance of these nanocarriers has experienced substantial growth and advancement alongside the rapid progress in the field of nanoscience. They demonstrate effective biocompatibility, biodistribution, and highly targeted delivery capabilities, making their particle size uniformity a crucial factor in enhancing both bioavailability and the overall drug-carrying capacity. Within the realm of organic nanocarriers, which encompass a variety of structures such as liposomes, polymer particles, and dendrimers, there are prevailing challenges related to toxicity, drug leakage, and the stability of the systems. Conversely, inorganic nanocarriers, which include materials like silica, metal nanoparticles, and quantum dots, are celebrated for their exceptional biocompatibility, the ease with which their surfaces can be modified, and remarkable stability. However, it is worth noting that their relatively high density may impose limitations on their overall efficacy in the intricate processes of drug delivery [3, 4].

#### **Importance of Targeted Drug Delivery**

Targeted drug delivery has become increasingly important in recent years, more than ever before. Understanding the limitations of classical systemic administration of therapeutic agents presents an opportunity for the development of a next generation of drug delivery vectors that can improve the pharmaceutical effects of drugs while at the same time reducing their side effects. Targeted drug delivery systems have shown a broad range of applications in improving the efficacy and safety of diagnostic agents and therapeutic drugs. However, translation of these novel drug targeting procedures to clinics is still largely hampered by manufacturing, safety, and biological barriers. A better understanding of biology-oriented target identification, design of new drug carriers, and screening of delivery efficacies is critical to advancing the development of targeted drug delivery systems. Efforts from multidisciplinary fields will make a significant impact on the clinical translation of these technologies. The conventional approaches to achieving drug targeting focus on the design of drug carriers with specific targeting moieties. A better understanding of the mechanism of cell-mediated targeting and the development of cell-based drug carrier systems provide new opportunities for drug targeting. Various strategies, including endogenous approach, immune modulation, contents, and surface modification, are currently being explored to design new cell-mediated targeting drug delivery systems. Efforts are needed to better constrain and standardize the design conditions and screening protocols for efficacy evaluations of these targeting drug delivery systems, which are expected to promote their clinical translation [5, 6].

#### **Nanoparticles In Drug Delivery**

There are several routes of administration and formulations on the market based on various delivery systems, such as liposomes, micelles, polymeric nanoparticles, covalent conjugates, and dendrimers. For the most part, they function based on the passive accumulation of the formulations in the tumor through the enhanced permeation and retention (EPR) effect, as seen for the very first batch of therapeutics. The concept of nanotechnology-based drug delivery systems has been firmly established, with various types of formulations currently on the market. Yet, the new era introduced various types of active targeting, stimuli-responsive, and thermoplastic design-based drug delivery systems. For the most part, these formulations are still in early preclinical development or in the late clinical development stages to obtain approval from the FDA. With these new systems, deeper genetic, epigenetic, and fold functionality analyses is feasible, active therapeutic strategies (and herewith new combinatorial strategies) can be successfully conducted, and new materials (also biomaterials) are discovered, potentially leading to better patient compliance and optimum therapeutic strategies. Traditional chemotherapy shows inefficacy against many types of cancer, as the drugs are so far too toxic to the body. Many studies on drug discovery have shown that it is likely there is a “type-based” drug that can target the most types of cancer cells based on a specific type of receptor. Efforts have been devoted to delivering sterically-hindered small molecules with the fruitless hope of discovering a new drug. A new drug delivery system with nanocarriers is now under thorough investigation to seek suitable candidates for the drug delivery system. Nano-sized liposomes with over 100 nm of diameters are used for drug delivery into circulation; on the other hand, polymeric and lipidic nanocarriers are employed to enter the tumor interstitium through passive targeting. Nanocarriers such as liposomes, polymeric, and lipidic nanoparticles have precisely recorded the history of drug delivery system development. The existence of blood vessels

diffuses in the tumor, but the diameter of the capillary is often bigger than 15 nm, enabling the passive targeting of nano-sized formulation through enhanced permeation [7, 8].

### **Mechanisms of Targeted Delivery**

In medicine, numerous potential mechanisms can be engineered to ensure that drugs are specifically delivered to diseased tissues and cells. For example, due to a cast range of characteristics, diseased tissues are usually referred to as “textbook” sites for passive drug targeting. On their part, cells express various receptors and transporters on their surface, which can serve as molecular anchors to draw the biomedical nanodevices to the cells. In this sense, classic approaches to rationally engineer active targeting capabilities for nanocarriers are to coat them with specific ligands that can establish the aforementioned end-point associations with specific cell targets. Many different biomedically relevant nanosized delivery vehicles have been successfully exploited to ferry diverse medicines, eventually leading to a groundbreaking paradigm shift in modern medicine. In this respect, nebulizer-ready solid carbon nano-compounds have drawn increasing attention for the nebulized delivery of drugs to the airways. Such nano-compounds can also be coated with various pharmaceutical formulations. However, both the nano-compounds and their drug-coated forms are generally agglomerated in tap water immediately after dispersion. This has depopulated a complete understanding of the mechanisms that drive nano-carrier-modulated drug two-dimensional initial contact and three-dimensional persistent dispersal. Nanomedicine is revolutionizing healthcare by delivering innovative drugs using nanocarriers such as liposomes, dendrimers, micelles, silica nanoparticles, carbon-based nanoparticles, etc. Many such nanosized delivery vehicles have been successfully exploited to ferry diverse medicines, eventually leading to a groundbreaking paradigm shift in modern medicine. While many new drugs released into the market are nano-formulations of old drugs, zero, or even negative, drug efficacy has not infrequently been reported for proprietary nano-formulations designed to outsmart the surrounding environment [9, 10].

### **Surface Modification of Nanoparticles**

Surface modification of nanoparticles, including simple physicochemical processes and bioorthogonal conjugation, to generate inhibitors and antifouling agents such as glycopolymer-based nanocarriers. Antibodies require 4–7 days to produce, and immunogenic responses to the confidence of protein molecule nanocarriers can lead to off-target biodistribution. Liquid nanoparticles have good photophysical properties, making them potential bio-labeling agents for bioimaging, but they should not attach strongly to protein molecules under physiological conditions. Dessicated emulsion systems are economical, and their powder turnover products have glassy states and exhibit good transportability and storage stability. Microorganisms are excellent biocatalysts, and lipid-derived cocci are resistant to extreme conditions of biocatalyst Coryne for the production of long-chain polyunsaturated fatty acids (PUFA). These PUFAs control vital physiological processes in the intended site of action (SOA) via endocytic uptake and enhance the potency of a post-encapsulated chemotherapeutic. By screening antifouling components, breast cancer-targeted drug delivery systems have been generated based on the nano-lamellae on amphiphilic graft copolymer-supported sylvic acid micelle, and amphiphilic glycopolymers have been designed to be well-stabilized nanoparticles that resist blood serum Protein adsorption. Antisense oligonucleotide transfection has been achieved by grafting oligo-lysines onto a block copolymer that combines polysarcosine and poly-L-phenylalanine nanoparticles, and polysarcosine-modified polymeric micelles for enhanced blood circulation and inhibited fouling of proteins have been synthesized. HSGCSM-PTX-HBc had reduced interactions with blood proteins, blocked the endocytic uptake pathway of proteins, and successfully targeted hepatic and cytoplasmic drug delivery [11].

### **Types of Targeted Drug Delivery Systems**

Nanoparticles, sized between 1 and 100 nm, include fullerenes, quantum dots, and carbon nanotubes, among others. Recent efforts focus on developing nanoparticles for therapeutic delivery. Polymer-based nanoparticles like liposomes and dendrimers have been effectively used in clinics to deliver therapeutic agents to cells. Inorganic nanoparticles (silica, gold, iron oxide) are employed for imaging and biosensing in vitro and in vivo. Armoured nanoparticles such as poly (1,6-hexamethylene biguanide)-based types enable controlled release of antibacterial agents. Nanoparticles function as carriers for theranostic agents (including gold and silica nanoparticles), facilitate co-delivery of therapies to enhance efficacy while reducing side effects (e.g., silver nanoparticles in drug coordination), and enable organelle-targeted delivery (e.g., gold ladder and mesoporous silica nanoparticles). They also support bio-detection and imaging for theranostic assessments (e.g., europium-doped silica nanoparticles). The EPR effect drives passive accumulation of nanoparticles in tumors. Some nanoparticles feature ligands or antibodies for the

specific targeting of diseased tissues. Cellular uptake mechanisms include clathrin-mediated endocytosis and membrane fusion, with developments in sub-diffractive nanoprobes to monitor these processes. Advanced imaging techniques have improved time-lapse resolution, utilizing surface-capped gold nanoparticles in live cell photothermal monitoring and investigating PAMAM dendrimer systems through NIR fluorescence and magnetic resonance imaging [12, 13].

#### **Applications In Cancer Therapy**

The application of nanoparticles (NPs) in drug delivery is gaining attention in cancer therapy due to their unique properties that allow for the tailored design of size, shape, and charge. Despite this, challenges with drug loading, biocompatibility, and biodegradability hinder the development of NP-based carriers. Various research groups are addressing these issues by creating innovative nanoplateforms. Some systems utilize reaction-triggered mechanisms to convert prodrugs and drug carriers simultaneously into active forms, enhancing the efficacy of delivery while allowing real-time monitoring through fluorescence. Nanocarriers that co-encapsulate drugs with fluorescent probes have shown increased precision in targeted cancer therapy and monitoring. This review highlights NPs' applications in cancer treatment, particularly NP-based carriers for accurate drug delivery. As nanotechnology advances in medicine, its role in cancer treatment becomes more significant. The American Cancer Society estimated over 1.7 million new cancer cases in the U.S. by 2018, with lung cancer being the leading cause of death. Current primary therapies include surgery, radiation therapy (RT), and chemotherapy. Surgery is effective in early-stage cancers with clear margins but has limitations with metastasized tumors. When surgery is insufficient, chemotherapy and RT are the preferred treatments, with chemotherapy often following surgery to prevent metastasis [14, 15].

#### **Applications in Gene Therapy**

Gene therapy is proposed as a means of preventing or treating genetic disease by modifying the diseased genetic processes. Dengue virus is a virus-borne disease that is becoming a worldwide health concern. An anti-DENV infection gene, interferon- $\alpha 2a$ , was successfully delivered by nanocarriers in a GSEA model. Hybrid gene delivery vectors combining the merits of viral DNA and nonviral polycation were developed to efficiently deliver DNA into neurons. Other d-NA-based anticancer materials, including DNA-based inhibitors of Aptamers, DNA enzymes, and DNA nanocarriers or switches, were applied in targeted cancer therapies. Some other genes, including RNAi-based genes, were delivered by nanoparticles against sustained-release delivery, targeted delivery, combinatory gene and protein delivery, and simulating the function of calcium homeostasis mechanisms. These advances indicate that NP-based in vivo gene delivery approaches are approaching clinics and will impact human medicine. Cancer is a chief contributor to death worldwide. Gene therapy emerged as a new treatment modality that makes use of genetic materials to treat human disease by transferring genetic material into the cells. Gene therapy has great potential in the treatment of cancer, as genetic mutation has been recognized as a major cause of cancer. Gene transfer has been greatly advanced by the development of viral and nonviral gene delivery carriers. Among them, the nanotechnology-based NP-gene delivery systems have received significant attention in anticancer therapies for their potential advantages of high gene delivery efficiency and low side effects. This review summarizes recent advances in NP-based anticancer gene therapy treatment. In particular, recent advances in NP and vector technology for anticancer gene delivery applications are discussed, with special emphasis on the development of cationic NPs as nonviral gene delivery carriers. In addition, some examples of anticancer gene therapy-agent drug combinations are also highlighted [16, 17].

#### **Challenges In Targeted Drug Delivery**

The emergence of drug-targeting strategies utilizing nanosized carriers has ignited long-standing hope for sharpening drug delivery and improving the efficacy of drugs while limiting side effects. Interest in utilizing particle targeting for drug delivery purposes exploded after the demonstration of tumor accumulation of nano-sized compounds due to the enhanced permeability and retention (EPR) effect. The use of nano-sized delivery systems for drug-targeting purposes has led to the development of nanosized drug carriers (nanomedicines) of variable size and composition. Structural characteristics of nanomedicines, such as size, shape, and composition, largely determine the pharmacokinetics of nanomedicines, i.e., circulation time in plasma, accumulation in specific tissues, and transfer into cells. About tumor targeting, cancer therapeutics are typically associated with "passively" targeting liposomes exploiting the EPR effect. Nevertheless, other delivery systems, such as pegylated liposomal doxorubicin and RNA-interference containing lipid nanoparticles, rely on active targeting mechanisms that partly involve carrier modification. Remarkable progress in drug-targeting strategies has provided hope for the

availability of highly targeted drugs. However, despite the seemingly large number of drug delivery systems and a plethora of preclinical data irrefutably demonstrating their potential, only a handful of nano-drugs have found their way into humans. Consequently, real proof-of-principle for targeting with nanomedicines is scant and is mostly limited to studies utilizing meriting antibody-drug conjugates or relying on passive mechanisms targeting the liver. Serious hurdles limit the opportunities for drug delivery systems with prolonged circulation times and tumor targeting efficacy in patients. Significant research challenges are involved in enhancing drug delivery to solid tumors, allowing the exploration of the potential of this approach in patients [18, 19].

#### **Future Perspectives**

Nanotechnology is revolutionizing drug delivery systems by optimizing dosing and targeting, improving efficiency, and patient compliance. Ongoing research explores various approaches to enhance targeted drug delivery, influenced by factors like age and health. Each drug administration method has advantages and limitations. The oral route is convenient but often ineffective due to drug breakdown in the stomach and gut. Skin hydrogels perform better than ointments for dermatological treatments, while topical applications are mainly used for skin infections. Insulin, being polar, requires intravenous delivery instead of oral, while rectal administration is common for treating nausea in children. Inhalation is frequently used for conditions like asthma. However, current methods are often ineffective and are poised for transformation via nanotechnology, which aims to create nanodrugs that target specific tissues, minimizing side effects. Understanding nanosystems and their biological interactions is crucial for effective delivery. Overcoming challenges such as drug stability and bioavailability is vital; factors like degradation within cells and alterations in drug-binding receptors impact efficacy. The introduction of modified drug carriers through nanotechnology will advance drug measurement and tracking in the body. New methodologies will assess the pharmacokinetics and metabolism of these nanoparticles, ensuring effective monitoring of drug concentrations and therapeutic targets. Eventually, the focus will shift to the development of smart, multifunctional nanomaterials for therapeutic use [20, 21].

#### **Case Studies**

Nanoparticles exhibit unique properties that differ from individual atoms and bulk matter, making them a focal point in pharmaceutical research, particularly for cancer therapy. They enhance the delivery of chemotherapeutic agents to tumors while minimizing toxicity to healthy tissues, using passive targeting through the enhanced permeability and retention effect, or active targeting via specific ligands like antibodies or peptides. Common nanoparticles include liposomes, micelles, dendrimers, and others, many of which are in clinical trials or on the market. Recent advancements allow for the design of nanocarriers in line with precision medicine, delivering tailored therapeutics based on tumor genetics. These nanoparticles facilitate targeted drug delivery, improve the uptake of poorly soluble medications, enhance targeting, and increase drug bioavailability. Anti-cancer drugs such as methotrexate, tamoxifen, and doxorubicin have been effectively formulated using nanomaterials. The efficacy of these nanosystems has been validated through in vitro and in vivo studies. Dexamethasone, a key chemotherapeutic agent, requires efficient cellular entry for its anti-proliferative and anti-inflammatory actions. Nanoparticle-assisted delivery significantly enhances its effectiveness, promoting normal function in aortic smooth muscle cells and improving cardiac function in heart failure models by reducing interstitial fibrosis. Colloidal drug delivery systems like liposomes and micelles have been extensively studied, focusing on passive and active targeting. Active targeting involves specific ligands that bind to cancer cell receptors. The success of these delivery systems depends on their small size for efficient permeability, reduced toxicity, controlled drug release, and optimized pharmacokinetics. Other strategies include developing nanocrystals and biocompatible polymeric micelles to encapsulate poorly soluble drugs [22, 23, 24, 25, 26, 27, 28].

#### **Ethical Considerations**

Future applications of nanotechnology may include nanoparticles for early disease detection and therapeutic delivery. The vision is for nanoparticles to accurately target areas within the body for localized drug release, minimizing systemic side effects commonly associated with general drug therapy. These advances could vastly improve treatments for serious diseases, including cancer and Alzheimer's. However, introducing new technologies raises unforeseen risks, paralleling past technology introductions, and highlights the need for ethical considerations in nanoparticle applications in medicine. For instance, a patient with advanced cancer could benefit from targeted drug delivery via nanoparticles, assuming their efficacy. These nanoparticles, or nanosystems, have been developed globally, primarily in

military research, leaving questions about their safety in human use. Understanding patient care in this context underscores the potential of nanoparticles for drug delivery and early disease detection. Numerous engineered systems are available for diagnostics and therapy, with therapeutic agents encapsulated or attached to nanocarriers, addressing drug solubility challenges. Their small size allows for targeted delivery to specific cells post-injection, potentially enhancing therapeutic outcomes while reducing side effects. However, we must remain cognizant of the possible toxicity associated with nanoparticles due to their nanoscale dimensions, acknowledging risks such as adverse interactions with biological systems and the environment. Thus, a thorough risk-benefit analysis is essential [24, 25].

### CONCLUSION

The integration of nanotechnology into medicine has significantly advanced the design and implementation of targeted drug delivery systems, providing a promising route to overcome many limitations of traditional therapies. Nanocarriers offer enhanced biocompatibility, controlled release, and improved targeting capabilities, which are critical for the treatment of complex diseases such as cancer and genetic disorders. However, despite impressive preclinical results, the translation of these systems into widespread clinical practice faces challenges, including issues related to safety, efficacy, and large-scale production. Addressing these obstacles demands interdisciplinary collaboration and innovative engineering of nanomaterials with multifunctional capabilities. Future research must focus on understanding biological interactions at the nanoscale, optimizing delivery mechanisms, and developing standardized protocols to evaluate efficacy and safety. With continued progress, nanotechnology holds the potential to redefine therapeutic strategies, ushering in a new era of personalized and precision medicine.

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